

Amendment to the Drawing

The attached sheets of drawings include changes to Figures 1, 2 and 6. These sheets replace the original sheets. In Figures 1, 2, and 6, sequence ID numbers have been added to identify the sequences shown.

Attachment: Replacement Sheets 1-19

Remarks/Arguments

Claim 1 has been amended to recite additional characteristics of the alien probe. Support for this amendment is found in paragraph [39] through paragraph [42] of the application.

New claims 4-8 have been added. Support for new claims 4 and 5 is found in the second to last sentence of paragraph [41]. Support for new claim 6 is found in the first sentence of paragraph [42]. Support for new claims 7 and 8 is found in Figures 1 and 2, respectively.

No new matter has been added as a result of these amendments.

Drawings

Replacement drawing sheets are attached. The amended Figures 1, 2 and 6 include SEQ ID numbers identifying the appropriate sequences.

Sequence Listing

Paragraphs 132 and 137 of the specification have been amended to include SEQ ID NOs 151-153 that identify the disclosed sequences.

A sequence listing in compliance with 37 CFR 1.821 through 1.825 is attached in both paper and computer-readable form, along with an amendment introducing the sequence listing, and a statement under 37 CFR 1.821.

Applicant notes that:

- 1) SEQ ID NOs: 148-153 have been concatenated into a single sequence, SEQ ID NO: 148;
- 2) SEQ ID NOs: 154-158 have been concatenated into a single sequence, SEQ ID NO: 149; and
- 3) SEQ ID NOs: 159-163 have been concatenated into a single sequence, SEQ ID NO: 150.

Rejections under 35 USC §102

Schena et al.

Claims 1 and 2 have been rejected under 35 USC §102(b) as being anticipated by Schena *et al.* (PNAS, Vol. 93, pages 10614-10619, October 1996).

Schena *et al.* teach parallel human cDNA arrays that use *Arabidopsis* nucleic acids as hybridization controls. The Examiner asserts that the *Arabidopsis* controls are alien to the array of Schena *et al.* since they are not normally present in human cDNAs samples. Although Applicant disagrees with the previously levied rejection, claim 1 has been amended to recite, in pertinent part, that the alien probe of claim 1 does not occur naturally in any organism. Furthermore, claim 1 has been amended to recite that sequence of the alien probe is generated by applying a modified Hidden Markov algorithm in which a sequence statistic of the one or more naturally-occurring sequences of interest is switched at an adjustable frequency to a sequence statistic that is inversely proportional to the natural sequence statistic, such that the alien sequence comprises intermittent highly improbable sequence patterns or subsequences throughout its length. Such an algorithm is neither taught nor suggested by Schena *et al.*

Thus, the teachings of Schena *et al.* do not anticipate, or render obvious, currently amended claim 1 or its dependent claims and Applicant respectfully requests withdrawal of this rejection.

Bao et al.

Claims 1 and 2 have been rejected under 35 USC §102(b) as being anticipated by Bao *et al.* (US Patent No. 6,251,601, June 2001). The Examiner asserts that Bao *et al.* anticipate the instant claims since Bao *et al.* measure human gene expression using nucleic acid arrays that contain a reference spot of lambda phage DNA.

Bao *et al.* teach hybridization arrays using at least one reference nucleic acid molecule. In column 12, lines 30-40, Bao *et al.* teach that “the reference nucleic acid population is any suitable nucleic acid collection chosen to serve as a reference. For example, the reference population can be total human genomic DNA from normal tissue, total mRNA extracted from a normal sample of the tissue to be tested and converted to cDNA, or a synthetic or naturally-occurring mixture of cDNA for particular expressed genes. The reference can be a cRNA population. The reference also can include a ‘spiked,’ known amount of a particular genomic or cDNA sequence to enable control analysis.”

Bao *et al.* fail to teach or suggest that their reference nucleic acid molecule is generated by a modified Hidden Markov algorithm in which a sequence statistic of the one or more naturally-occurring sequences of interest is switched at an adjustable frequency to a sequence

statistic that is inversely proportional to the natural sequence statistic, such that the alien sequence comprises intermittent highly improbable sequence patterns or subsequences throughout its length, as recited in currently amended claim 1. Although Applicant disagrees with the previously levied rejection, the current amendments to claim 1 render this rejection moot.

Thus, the teachings of Bao *et al.* do not anticipate, or render obvious, currently amended claim 1 or its dependent claims and Applicant respectfully requests withdrawal of this rejection.

Shah

Claims 1 and 2 have been rejected under 35 USC §102(e) as being anticipated by Shah (US Patent No. 6,916,621, July 2005). The Examiner asserts that Shah anticipates the instant claims since Shah employs arrays containing “calibration molecules” for normalizing results of array-based binding assays.

Shah primarily teaches an equimolar mixture of each nucleic acid that is spotted on the array to provide normalization. Shah also states on column 22, lines 16-24, that, “In another aspect, the calibration spot(s) use nucleic acid from genomes other than that spotted on the array. For example, in one aspect, human genomic DNA is used in the ‘test spots’ (for, e.g., human genomic CGH) and the calibration spot(s) are non-human nucleic acid, e.g., the genomic DNA from Mus, Drosophila or equivalent. Thus, some or all of the ‘test spots’ would include at least one ‘marker’ Drosophila (or equivalent) sequence also on a ‘calibration spot.’”

Thus, like Schena *et al.*, Shah teaches only naturally occurring nucleic acid sequences as “calibration molecules”. Claim 1 has been amended to recite that the alien probe of claim 1 does not occur naturally in any organism.

Furthermore, claim 1 has been amended to recite that the alien probe is generated by applying a modified Hidden Markov algorithm in which a sequence statistic of the one or more naturally-occurring sequences of interest is switched at an adjustable frequency to a sequence statistic that is inversely proportional to the natural sequence statistic, such that the alien sequence comprises intermittent highly improbable sequence patterns or subsequences throughout its length, a feature neither taught nor suggested by Shah. Although Applicant disagrees with the previously levied rejection, the current amendments to claim 1 render this rejection moot.

Therefore, Shah does not anticipate, or render obvious, currently amended claim 1 or its dependent claims and Applicant respectfully requests withdrawal of this rejection.

Kincaid

Claims 1-3 have been rejected under 35 USC §102(e) as being anticipated by Kincaid (US Patent Application Publication No. 2003/0186310, October 2003). The Examiner asserts that Kincaid anticipates the instant claims since Kincaid employs arrays containing “control probes” at each “feature” (analogous to the “discrete location” recited in the instant claims) on the array, wherein the control probes do not interfere with hybridization of a target sequence. Kincaid defines a “control probe” as “an oligonucleotide or oligomer having a known sequence of nucleotides in a known quantity, which is statistically known not to hybridize or otherwise interfere with an oligomer test probe or target sample under test.”

Although Applicant disagrees with the previously levied rejection, claim 1 has been amended to recite, in pertinent part, that the alien probe is generated by a modified Hidden Markov algorithm in which a sequence statistic of the one or more naturally-occurring sequences of interest is switched at an adjustable frequency to a sequence statistic that is inversely proportional to the natural sequence statistic, such that the alien sequence comprises intermittent highly improbable sequence patterns or subsequences throughout its length. Such an algorithm is neither taught nor suggested by Kincaid.

Thus, the teachings of Kincaid do not anticipate, or render obvious, currently amended claim 1 or its dependent claims and Applicant respectfully requests withdrawal of this rejection.

Applicant submits that the present amendment and arguments place this application in condition for allowance. A notice to that effect is respectfully requested.

Applicant thanks the Examiner for careful consideration of this case. Please charge any fees that may be associated with this matter, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,



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